

AMENDMENTS TO THE CLAIMS

1. (Withdrawn) A method of detecting proliferative diseases causing sclerosis, comprising measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1, phosphorylated Smad1, activin receptor-like kinase 1, activin receptor-like kinase 3 and bone morphogenetic proteins in a biological sample.

2. (Withdrawn) A method of evaluating the degree of progress and/or the efficacy of treatment of proliferative diseases causing sclerosis, comprising measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1, phosphorylated Smad1, activin receptor-like kinase 1, activin receptor-like kinase 3 and bone morphogenetic proteins in a biological sample.

3. (Withdrawn) A kit for detecting proliferative diseases causing sclerosis, comprising a reagent(s) for measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1, phosphorylated Smad1, activin receptor-like kinase 1, activin receptor-like kinase 3 and bone morphogenetic proteins in a biological sample.

4. (Withdrawn) A kit for evaluating the degree of progress and/or the efficacy of treatment of proliferative diseases causing sclerosis, comprising a reagent(s) for measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1, phosphorylated Smad1, activin receptor-like kinase 1, activin receptor-like kinase 3 and bone morphogenetic proteins in a biological sample.

5. (Withdrawn) A method of detecting diabetic nephropathy, comprising measuring the expression of Smad1 and/or a substance having Smad1-activating effect in a biological sample.

6. (Withdrawn) A method of evaluating the degree of progress and/or the efficacy of treatment of diabetic nephropathy, comprising measuring the expression of Smad1 and/or a substance having Smad1-activating effect in a biological sample.

7. (Withdrawn) A kit for detecting diabetic nephropathy, comprising a reagent(s) for measuring the expression of Smad1 and/or a substance having Smad1-activating effect.

8. (Withdrawn) A kit for evaluating the degree of progress and/or the efficacy of treatment of diabetic nephropathy, comprising a reagent(s) for measuring the expression of Smad1 and/or a substance having Smad1-activating effect.

9. (Withdrawn) A prophylactic and/or therapeutic agent for proliferative diseases causing sclerosis, comprising as an active ingredient a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

10. (Withdrawn) A drug inhibiting the increase of extracellular matrix, comprising as an active ingredient a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

11. (Withdrawn) A drug inhibiting the expression of $\alpha 1$ type IV collagen, comprising as an active ingredient a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

12. (Currently Amended) A method of identifying an agent ~~substances~~ effective in preventing and/or treating a proliferative diseases ~~disease~~ causing sclerosis, comprising judging whether or not contacting a test substance agent with a biological sample;

determining the level of expression ~~inhibits the expression~~ of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1 in the biological sample in comparison to the level of expression of the substance in a control sample;

wherein a decrease in expression of STAT3, phosphorylated STAT3, Smad1 or phosphorylated Smad1 in comparison to the expression level of the substance in the control sample indicates the agent is effective in the prevention and/or treatment of proliferative diseases causing sclerosis.

13. (Currently Amended) A method of identifying substances an agent effective in inhibiting the increase of extracellular matrix, comprising

judging whether or not contacting a test substance agent with a biological sample;

determining the level of expression ~~inhibits the expression~~ of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1 in the biological sample in comparison to the level of expression of the substance in a control sample;

wherein a decrease in expression of STAT3, phosphorylated STAT3, Smad1 or phosphorylated Smad1 in comparison to the expression level of the substance in the control sample indicates the agent is effective in inhibiting the increase of extracellular matrix.

14. (Currently Amended) A method of identifying substances effective in inhibiting the expression of $\alpha 1$ type IV collagen, comprising

judging whether or not contacting a test substance agent with a biological sample;

determining the level of expression ~~inhibits the expression~~ of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1 in the biological sample in comparison to the level of expression of the substance in a control sample,

wherein a decrease in expression of STAT3, phosphorylated STAT3, Smad1 or phosphorylated Smad1 in comparison to the expression level of the substance in the control sample indicates the agent is effective in inhibiting the expression of $\alpha 1$ type IV collagen.

15. (Withdrawn) A kit for identifying substances effective in preventing and/or treating proliferative diseases causing sclerosis, comprising a reagent(s) for measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

16. (Withdrawn) A kit for identifying substances effective in inhibiting the increase of extracellular matrix, comprising a reagent(s) for measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

17. (Withdrawn) A kit for Identifying substances effective in inhibiting the expression of $\alpha 1$ type IV collagen, comprising a reagent(s) for measuring the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

18. (Withdrawn) A method for producing a prophylactic and/or therapeutic effect on proliferative diseases causing sclerosis, comprising administering to a subject a drug including a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

19. (Withdrawn) A method of inhibiting an increase of extracellular matrix, comprising administering to a subject a drug including a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

20. (Withdrawn) A method of inhibiting an increase of extracellular matrix, comprising providing to a sample a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

21. (Withdrawn) A method of inhibiting an expression of $\alpha 1$ type IV collagen, comprising administering to a subject a drug including a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

22. (Withdrawn) A method of inhibiting an expression of $\alpha 1$ type IV collagen, comprising providing to a sample a substance having an inhibitory effect on the expression of at least one substance selected from the group consisting of STAT3, phosphorylated STAT3, Smad1 and phosphorylated Smad1.

23. (Withdrawn) A method of claim 18, wherein the substance to be administered includes antisense oligonucleotides to Smad1, Smad1 Antagonistic Effector, an anti-PDGF β receptor antibody, or antisense oligonucleotides to STAT3.

24. (Withdrawn) A method of claim 18, wherein the substance to be administered has a sequence comprising SEQ ID NO: 13.

25. (New) The method of any one of claims 12, 13, or 14, wherein the biological sample is selected from the group consisting of renal tissue sections, blood, sera and urine.

26. (New) The method of any one of claims 12, 13, or 14, wherein the biological sample is selected from mesangial cells.

27. (New) The method of any one of claims 12, 13, or 14, wherein the level of expression is measured at the nucleic acid level or the protein level.

28. (New) The method of claim 12, wherein the proliferative disease causing sclerosis is a renal disease which damages glomeruli.

29. (New) The method of claim 12, wherein the proliferative disease causing sclerosis is selected from the group consisting of diabetic nephropathy, chronic glomerulonephritis, membranous proliferative glomerulonephritis, focal glomerulosclerosis, light chain disease, cryoglobulinemic nephritis, HIV-associated nephritis, purpuric nephritis, hepatic fibrosis, and arteriosclerosis.

30. (New) The method of any one of claims 12, 13, or 14, wherein the level of expression of phosphorylated STAT3, Smad1 or phosphorylated Smad1 at the nucleic acid level is measured using primer pairs selected from SEQ ID NOS. 21 and 22, or SEQ ID NOS. 5 and 6.

31. (New) The method of any one of claims 12, 13, or 14, wherein the level of expression of phosphorylated STAT3, Smad1 or phosphorylated Smad1 at the protein level is measured by Western Blotting, ELISA or immunohistochemical analysis.